No. 2013-1406

IN THE

United States Court of Appeals for the Federal Circuit

TAKEDA PHARMACEUTICAL COMPANY LIMITED,
TAKEDA PHARMACEUTICALS NORTH AMERICA, INC.,
TAKEDA PHARMACEUTICALS, LLC,
TAKEDA PHARMACEUTICALS AMERICA, INC.,
and ETHYPHARM, S.A.,

Plaintiffs-Appellees,

v.

ZYDUS PHARMACEUTICALS USA, INC.,
and CADILA HEALTHCARE, LIMITED,

Defendants-Appellants.

Appeal from the United States District Court
for the District of New Jersey
Case No. 3:10-cv-1723
District Judge Joel A. Pisano

NONCONFIDENTIAL BRIEF FOR APPELLEES

Eric J. Lobenfeld
Arlene L. Chow
HOGAN LOVELLS US LLP
875 Third Avenue
New York, NY 10022
(212) 918-3000

Catherine E. Stetson
Frederick Liu
HOGAN LOVELLS US LLP
555 Thirteenth Street, N.W.
Washington, D.C. 20004
(202) 637-5600

August 29, 2013

Counsel for Appellees

CERTIFICATE OF INTEREST

Counsel for appellees hereby certifies as follows:

1. The full name of every party represented is: Takeda Pharmaceutical Co. Ltd., Takeda Pharmaceuticals North America, Inc., Takeda Pharmaceuticals LLC, Takeda Pharmaceuticals America, Inc., and Ethypharm, S.A.

2. The real parties in interest are: Takeda Pharmaceutical Co. Ltd., Takeda Pharmaceuticals U.S.A., Inc., Takeda Pharmaceuticals LLC, Takeda Pharmaceuticals America, Inc., and Ethypharm, S.A.

3. All parent corporations and any publicly held companies that own 10% or more of the stock of the parties I represent are as follows:

a. Takeda Pharmaceutical Co. Ltd. No company owns 10% or more of the stock of Takeda Pharmaceutical Co. Ltd.

b. Takeda Pharmaceuticals North America, Inc. Takeda Pharmaceuticals North America, Inc., has changed its name to Takeda Pharmaceuticals U.S.A., Inc. Takeda Pharmaceuticals U.S.A., Inc., is a wholly owned subsidiary of Takeda America Holdings, Inc., which is a wholly owned subsidiary of Takeda Pharmaceutical Co. Ltd.

c. Takeda Pharmaceuticals LLC. Takeda Pharmaceuticals LLC is owned by Takeda Pharmaceuticals U.S.A., Inc., and its wholly owned subsidiary, Takeda Pharmaceuticals America, Inc. Takeda Pharmaceuticals U.S.A., Inc., is a

CERTIFICATE OF INTEREST – Continued

wholly owned subsidiary of Takeda America Holdings, Inc., which is a wholly owned subsidiary of Takeda Pharmaceutical Co. Ltd.

d. Takeda Pharmaceuticals America, Inc. Takeda Pharmaceuticals America, Inc., is a wholly owned subsidiary of Takeda Pharmaceuticals U.S.A., Inc., which is a wholly owned subsidiary of Takeda America Holdings, Inc., which is a wholly owned subsidiary of Takeda Pharmaceutical Co. Ltd.

e. Ethypharm, S.A. Ethypharm, S.A., is 99.09% owned by Financiere Verdi, and no publicly held corporation owns 10% or more of Ethypharm's stock.

4. The names of all law firms and partners or associates that appeared for the parties represented by me in the trial court or that are expected to appear in this court are:

Hogan Lovells US LLP: Eric. J. Lobenfeld, Catherine E. Stetson, Arlene L. Chow, Dillon Kim, Frederick Liu, Peter Noh, Bonnie Chen, Takashi Okuda.

Hogan Lovells Horitsu Jimusho: Philippe Y. Riesen.

McCarter & English, LLP: Carissa L. Rodrigue, Elina Slavin, John Edmund Flaherty, Jonathan M.H. Short, Mark A. Anania, Symone J. Redwine, William J. Heller.

Baker Botts LLP: Paul A. Ragusa, Lisa Kole, Sandra Lee.

/s/ Catherine E. Stetson
Catherine E. Stetson

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CONFIDENTIAL MATERIAL OMITTED

The material omitted throughout this brief relates to Zydus's ANDA product, Zydus's communications with the Food and Drug Administration, and the basis for certain proprietary business decisions made by Zydus. That material is confidential and subject to a protective order in the District Court.

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STATEMENT OF RELATED CASES

Pursuant to Federal Circuit Rule 47.5, counsel for appellees states that an appeal in the same civil action in the District Court was previously before this Court in *Takeda Pharmaceutical Co.* v. *Zydus Pharmaceuticals USA, Inc.*, No. 2013-1089. In that appeal, Zydus sought review of an interlocutory order extending the statutory period during which any approval of its abbreviated new drug application by the Food and Drug Administration could not become effective. This Court did not render a decision on the merits of the appeal, because the parties agreed to voluntarily dismiss the appeal before oral argument. This Court granted the parties' joint motion for voluntary dismissal in an unpublished and nonprecedential order signed by the Clerk of the Court on February 7, 2013.

Counsel for appellees are not aware of any case pending in this or any other court that will directly affect or be directly affected by this Court's decision in the pending appeal. There is, however, a case pending in the U.S. District Court for the District of New Jersey involving the same patent. *See Takeda Pharm. Co. Ltd.* v. *Lupin Ltd.*, No. 3:12-cv-07333 (D.N.J. filed Nov. 29, 2012).

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CONFIDENTIAL
BRIEF FOR APPELLEES

JURISDICTION

The District Court had jurisdiction in this patent case under 28 U.S.C. § 1338(a). The District Court entered final judgment on May 7, 2013. JA 104-105.

Appellants filed a notice of appeal on May 9, 2013. JA 56. This Court has jurisdiction under 28 U.S.C. § 1295(a)(1).

COUNTERSTATEMENT OF THE ISSUES

The patent at issue in this case claims pharmaceutical tablets containing fine granules of a certain average particle diameter. The District Court construed the patent to cover fine granules with an average particle diameter of 440 µm or less. At a subsequent bench trial, appellees presented evidence that the average particle diameter of the fine granules in appellants' product is less than 440 µm. Based on that evidence, the District Court found that appellants' product infringed the patent. The court also concluded that appellants had not presented clear and convincing evidence that the patent is invalid.

The issues presented are:

1. Whether, on clear-error review, the District Court correctly found that appellants' product infringed the patent, where the only evidence of actual testing presented at trial showed that the fine granules in appellants' product have an average particle diameter of less than 440 µm.

2. Whether the District Court correctly held that appellants did not present clear and convincing evidence that the patent is invalid.

COUNTERSTATEMENT OF THE CASE

Appellees Takeda Pharmaceutical Company Limited, Takeda Pharmaceuticals U.S.A., Inc., Takeda Pharmaceuticals, LLC, and Takeda Pharmaceuticals America, Inc. (collectively, "Takeda") own patents that claim the

formulation for the brand-name drug Prevacid® SoluTab™. District Court's Docket Index ("DI") 98, at 5-6. Appellee Ethypharm, S.A., also owns a patent that covers that formulation. *Id.*

In 2010, appellants Zydus Pharmaceuticals USA, Inc., and Cadila Healthcare, Limited (together, "Zydus") filed an abbreviated new drug application ("ANDA") with the Food and Drug Administration, seeking to manufacture a generic version of Prevacid® SoluTab™. JA 60. Takeda and Ethypharm sued Zydus for patent infringement in federal district court, and Zydus counterclaimed, asserting non-infringement and challenging the validity of the patents. The parties subsequently withdrew their claims and counterclaims with respect to all patents except U.S. Patent No. 6,328,994 ("the '994 patent"), owned by Takeda. JA 60-61.

After a bench trial, the District Court issued a 46-page opinion finding that if Zydus's generic product were put on the market, it would infringe Claim 1 of the '994 patent. JA 103. The District Court also concluded that Zydus had not established by clear and convincing evidence that Claim 1 is invalid. JA 103. The District Court entered final judgment for Takeda, and Zydus now appeals. JA 104-105.

COUNTERSTATEMENT OF THE FACTS

In 2002, Takeda obtained FDA's approval to make and sell a new drug to treat gastroesophageal reflux disease ("GERD"), among other things. GERD is a

disease involving the digestive process. When a person eats, food passes from the mouth, down the esophagus, and to the stomach. The stomach produces acid to help digest the food, and a muscle connecting the esophagus to the stomach acts as a one-way valve preventing stomach acid from flowing back up the esophagus. JA 3685-3687. When someone has GERD, that valve does not work properly; acid enters the esophagus and causes irritation in the lining there. JA 3687. This acid reflux can lead to heartburn, ulcers, and—over time—even cancer. JA 3687-3689.

Takeda's product—marketed under the brand name Prevacid® SoluTab™—contains the active ingredient lansoprazole, which belongs to a class of drugs known as proton pump inhibitors ("PPIs"). JA 3689-3691. When PPIs are ingested, they are absorbed in the bloodstream and delivered to parietal cells in the stomach lining, where they block the proton pumps responsible for producing acid. JA 3689-3690. PPIs thus treat GERD by decreasing the amount of acid produced by the stomach in the first place. JA 3690.

Although PPIs have been the standard treatment for GERD for over ten years, Takeda's product is and has been the only PPI available in an orally disintegrating tablet ("ODT"). JA 101, 3689, 3691, 3696-3697, 4049. A patient takes an ODT not by swallowing or chewing it, but rather by allowing it to disintegrate in her mouth. JA 3691-3692. The tablet dissolves in less than a minute, leaving behind thousands of coated granules. *See* JA 125, 3692. Each

granule consists of a spherical core, covered with a layer of lansoprazole and then another layer of enteric coating. JA 3692-3693, 3719-3721. These granules the patient *does* swallow; the granules then make their way through the stomach to the small intestine, where the lansoprazole is released and absorbed into the bloodstream. JA 3692-3693. The enteric coating ensures that the lansoprazole reaches the small intestine intact, by preventing stomach acid from degrading the drug along the way. *Id.* For children, the elderly, and other patients who may have trouble swallowing traditional capsules, this ODT can be a life-changer, significantly improving their ability to deal with acid reflux. JA 3693-3696.

In 2010, Zydus filed an ANDA seeking FDA's approval to manufacture a generic version of Takeda's product. JA 60. Among other things, an ANDA must contain a certification with respect to each patent that claims the brand-name product or its use. 21 U.S.C. § 355(j)(2)(A)(vii). There are four patents that claim Takeda's product: three owned by Takeda, and one owned by Ethypharm. DI 98, at 5-6. Although each was once at issue in this case, the parties have at this point withdrawn their claims and counterclaims with respect to all but Claim 1 of the '994 patent, owned by Takeda. JA 60-61.

Zydus's ANDA contained a so-called "paragraph IV" certification, asserting that Claim 1 is invalid or would not be infringed by its generic product. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV). Under the patent statute, however, making a

paragraph IV certification is itself an act of infringement, giving the brand manufacturer an immediate right to sue. *See* 35 U.S.C. § 271(e)(2)(A). So in April 2010, Takeda sued Zydus, alleging, among other things, infringement of Claim 1, *see* DI 1, at 8-9; DI 98, at 8-9, which recites:

> An orally disintegrable tablet which comprises (i) *fine granules having an average particle diameter of 400 µm or less*, which fine granules comprise a composition coated by an enteric coating layer comprising a first component which is an enteric coating agent and a second component which is a sustained-release agent, said composition having 10 weight % or more of an acid-labile physiologically active substrate that is lansoprazole and (ii) an additive wherein said tablet having a hardness strength of about 1 to about 20 kg, is orally disintegrable.

JA 142 (emphasis added). Zydus counterclaimed, asserting that Claim 1 is invalid. DI 99, at 17.

During *Markman* claim-construction proceedings, the parties disputed the meaning of Claim 1's limitation regarding the size of the fine granules. Zydus argued that the limitation "400 µm or less" should be construed to mean "precisely 400 µm or less." JA 496. Takeda argued, based on the patent's specification and prevailing authorities on particle-size testing, that a person of ordinary skill in the art would instead understand the limitation to incorporate a ±10% deviation, to mean "400 µm (±10%) or less." JA 153-155. In an opinion issued in October 2011, the District Court agreed with Takeda. JA 112. That ruling meant that a generic product would literally infringe the '994 patent if it contained fine granules

with an "average particle diameter"—defined in the patent's specification as "median diameter," JA 70, 126—of 440 µm or less. Zydus moved for reconsideration. JA 1395. Zydus accepted that the particle-size limitation incorporated a deviation, but urged that the limitation be construed to "allow[] a variance in diameter of no more than ±3%." JA 1409. The District Court denied the motion, explaining that Zydus had merely "repeat[ed] a number of arguments that had earlier been presented to and evaluated by the Court." JA 1456.

The parties proceeded to engage in extensive discovery, including testing to measure the size of the fine granules in a batch of Zydus's ANDA product manufactured in 2009. JA 2115. But in September 2012—just weeks before trial was scheduled to begin—Zydus

JA 4551

(capitalization and boldface removed). Malvern is an instrument that measures the size of particles through laser diffraction: The instrument exposes particles to a laser beam; the particles diffract the laser, producing a radiation pattern; and from that pattern, the size of the particles can be inferred. JA 3736-3737, 3765. Laser diffraction is one standard method for measuring particle size in the pharmaceutical industry. JA 3738. But its limitations are widely known; if, for example, two granules are stuck together to form what is known as an agglomerate,

laser diffraction will measure them as one granule, not two. JA 3742-3743, 3853, 3951-3952.

Given the timing of Zydus's , the District Court granted Takeda's request to delay trial to permit the parties to conduct further discovery. JA 1457-1458. Takeda's expert in pharmaceutical formulation, Dr. David Bugay, then proceeded to test a new batch of Zydus's ANDA product—one reflecting the product Zydus would likely sell . JA 73-74, 79, 2772, 3721-3722, 3763-3765. Upon examining tablets from Zydus's new batch, Dr. Bugay found that about 20% of the particles inside were agglomerates. JA 3758-3759. So instead of using laser diffraction to measure particle size, Dr. Bugay used optical microscopy, another standard method. JA 3731, 3743-3744, 3882. Unlike laser diffraction, optical microscopy allows the user to distinguish between individual granules and agglomerates. JA 3742-3743, 3882. It works by generating actual images of the particles, divided into pixels; the user is then able to examine the image, determine whether a particle is composed of more than one granule, and calculate the diameter of each granule based on the number of pixels it occupies on the image. JA 3733-3734, 3743, 3750.

During a four-day bench trial in the spring of 2013, Takeda presented the results of Dr. Bugay's testing. Dr. Bugay sampled three tablets from Zydus's new batch, and used optical microscopy to measure all of the approximately 6,000

granules in each tablet. JA 3723. In doing so, he measured each granule individually, deagglomerating granules stuck together. JA 3751. Dr. Bugay found that the average particle diameter of the fine granules in each tablet was 413.76 µm, 426.94 µm, and 416.24 µm—which average to 418.98 µmper tablet. JA 3752. He then adjusted that figure upward to 420.46 µm, to account for granules potentially lost during the testing process. JA 3753-3755. Based on that adjusted figure, Dr. Bugay concluded that the average particle diameter of the fine granules of Zydus's ANDA product is less than 440 µm. JA 3755-3756.

In light of this evidence, the District Court found that Zydus's ANDA product infringes Claim 1 of the '994 patent. JA 78. The court found that a person of ordinary skill in the art would know to "deagglomerate prior to subjecting [a] sample to particle size testing," and so it agreed with Dr. Bugay's use of optical microscopy to measure the size of the "fine granules" in Zydus's ANDA product. JA 69, 77. The court then found, based on the results of Dr. Bugay's testing, that the fine granules in Zydus's ANDA product fall within Claim 1's particle-size limitation—and are therefore infringing. JA 77-78. The fact that Zydus

did not affect the court's conclusion. After all, the court explained, testing showed that the "fine granules" in Zydus's ANDA product have an average particle diameter *less* than 440 µm. JA 79-80. Moreover, Zydus's

did not resolve the question of infringement because it did not address two key issues: how to take account of agglomerates in Zydus's product, and how to collect representative samples of Zydus's granules for testing. JA 80.

The District Court also rejected Zydus's counterclaim that Claim 1 is invalid for alleged lack of enablement, lack of written description, and indefiniteness. JA 81-99. The court found that Zydus did not present clear and convincing evidence of invalidity on any of those grounds. JA 87, 88, 91, 98, 99.

Having found infringement of a valid patent, the court entered final judgment for Takeda. JA 104. The court enjoined Zydus from engaging in the commercial manufacture, use, or sale of its ANDA product until expiration of the '994 patent, in 2019. JA 105. And it ordered that the effective date of any FDA approval of Zydus's ANDA be no earlier than the expiration of the '994 patent and any applicable pediatric exclusivity. *Id.*

Zydus now appeals.

SUMMARY OF THE ARGUMENT

The judgment of the District Court should be affirmed. To begin, the District Court properly construed Claim 1's limitation of "fine granules having an average particle diameter of 400 µm or less" to incorporate a deviation of ±10%. Zydus does not dispute that the limitation should be read to incorporate *some* deviation; Zydus argues only that the deviation should be ±3%, not ±10%. But as

Zydus concedes, a ±3% deviation reflects only small instrument errors; it does not reflect other variances such as those inherent to the sample, associated with the user, or from measuring irregularly shaped particles. Because a person of ordinary skill in the art would understand the applicable deviation to be ±10%, the District Court's claim construction is correct.

Having properly construed the claim, the District Court did not clearly err in finding that Zydus's ANDA product would infringe it. The court found that a person of ordinary skill in the art would treat each individual, coated core as a "fine granule," deagglomerating any cores stuck together before measuring particle size. And actual testing showed that the average particle diameter of the individual, coated cores of Zydus's product is less than 400 µm plus 10%, or 440 µm—the upper limit of Claim 1. Zydus did not present any particle-size testing to the contrary. And although Zydus

does not resolve the infringement inquiry. That is because the

does not require deagglomeration or representative sampling of granules. As a result, Zydus could, based on its own faulty methodology, comply with its

and still infringe the patent—as the evidence of actual testing in this case showed.

Zydus's invalidity defense also fails. Zydus contends that Claim 1 is invalid for lack of enablement, but a person of ordinary skill could practice the invention without undue experimentation, using standard techniques to measure particle size. Zydus also argues that Claim 1 is invalid because it lacks a written description of the effect of compression forces during tableting, but the evidence showed that there was no such effect for the patent to describe. Finally, Zydus challenges Claim 1 as indefinite, arguing that the ±10% deviation incorporated into the claim construction renders the line between infringement and non-infringement ambiguous. But a person of ordinary skill would pay attention only to the +10%, knowing that the –10% is encompassed by the upper limit. Because Zydus did not present clear and convincing evidence establishing the invalidity of the patent, the District Court correctly rejected Zydus's defense.

ARGUMENT

I. THE DISTRICT COURT DID NOT CLEARLY ERR IN FINDING INFRINGEMENT.

"An infringement analysis involves two steps. First is claim construction—the scope and meaning of the patent claims asserted are determined. Second is determination of infringement—the properly construed claims are compared to the allegedly infringing product." *Clearstream Wastewater Sys., Inc.* v. *Hydro-Action, Inc.*, 206 F.3d 1440, 1444 (Fed. Cir. 2000) (citations omitted). "To establish literal infringement, every limitation set forth in a claim must be found in an accused

product, exactly." *Southwall Techs., Inc.* v. *Cardinal IG Co.*, 54 F.3d 1570, 1575 (Fed. Cir. 1995).

Here, Zydus concedes that its ANDA product embodies every limitation set forth in Claim 1 except one: the limitation "fine granules having an average particle diameter of 400 µm or less." JA 67-68. Thus, for purposes of infringement, the only question is whether that limitation is present in Zydus's ANDA product. As the District Court correctly found, the answer is yes.

A. The District Court Properly Construed The Patent To Cover Fine Granules With An Average Particle Diameter Of 440 µm Or Less.

Start with the first step: claim construction. A claim in a patent should be read through the eyes of a "person of ordinary skill in the art in question at the time of the invention." *Phillips* v. *AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). This means that in construing a claim, a court should aim to understand the inventor's words as would "a person in that field of technology." *Id.* (internal quotation marks omitted). And it means that in seeking that understanding, a court should consult the same materials as would that person: "the words of the claims themselves, the specification, the prosecution history, and any relevant extrinsic evidence." *Absolute Software, Inc.* v. *Stealth Signal, Inc.*, 659 F.3d 1121, 1129 (Fed. Cir. 2011) (citing *Phillips*, 415 F.3d at 1315-17).

Under existing circuit precedent, claim construction is a matter of law that this Court reviews de novo. *Cybor Corp.* v. *FAS Techs., Inc.*, 138 F.3d 1448,

1454-55 (Fed. Cir. 1998) (en banc). When reviewed de novo, the District Court's claim construction is correct. This Court, however, recently granted rehearing en banc to reconsider the appropriate standard of review in *Lighting Ballast Control LLC* v. *Philips Electronics North America Corp.* *See* 500 F. App'x 951, 951 (Fed. Cir. Mar. 15, 2013). In doing so, the Court may conclude that a claim construction should be reviewed under a more deferential standard when the district court relies on expert testimony or other evidence extrinsic to the patent. *See id.* at 952 (granting rehearing en banc to consider whether this Court should "afford deference to any aspect of a district court's claim construction," and "[i]f so, which aspects should be afforded deference"). If the Court so concludes, then the District Court's construction of Claim 1 would be entitled to deference in this case, because, as discussed below, it relies on similar evidence. Thus, under either standard of review, the court's construction should be affirmed.

The parties' dispute centers on the meaning of the term "400 µm or less." The District Court construed that term to incorporate a ±10% deviation. JA 67. And in doing so, the court rightly began with the patent itself. A patent's specification is "the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at 1315 (internal quotation marks omitted). When an inventor includes a "special definition" in the specification, "the inventor's lexicography governs." *Id.* at 1316.

Here, the inventors of the '994 patent did just that. They expressly defined the term "400 µm or less" in the specification: "In the present invention, 'fine granules having an average particle diameter of 400 µm or less, which fine granules comprise a composition coated by an enteric coating layer, said composition having 10 weight % or more of an acid-labile physiologically active substance' have an average particle diameter of *about* 400 µm or less, in order that roughness is not felt in the mouth." JA 126 (emphasis added). The inventors thus defined "400 µm" as an approximate figure. *See Sinorgchem Co.* v. *ITC*, 511 F.3d 1132, 1136 (Fed. Cir. 2007) (explaining that when a term in a patent "is set off by quotation marks," it is "often a strong indication that what follows is a definition"). And they repeated that definition throughout the specification. Another passage, for instance, states that "the average particle diameter of the included granules must be *about* 400 µm or less, preferably about 350 µm." JA 124 (emphasis added). And yet another passage says the same thing: "The 'fine granules' have an average particle diameter of *about* 400 µm or less, preferably 350 µm or less." JA 129 (emphasis added).

As the District Court rightly concluded, "the specification is clear that 'fine granules having a particle diameter of 400 µm or less' is not precise." JA 110. Because the specification defines "400 µm or less" to be "*about* 400 µm or less," a person of ordinary skill in the art would understand that the inventors did not

intend "400 µm" to be a strict upper limit. Rather, as the specification makes plain, the inventors intended the upper limit to be "*about* 400 µm."

This construction accords with evidence outside the patent. "[E]xtrinsic evidence in the form of expert testimony can be useful * * * to establish that a particular term in the patent * * * has a particular meaning in the pertinent field." *Phillips*, 415 F.3d at 1318. And here, Takeda presented expert testimony that a person of ordinary skill in the pertinent art would understand that the inventors did not intend "400 µm" to be precise. Both Dr. Bugay, an expert in pharmaceutical formulation, and Dr. Stephen Byrn, an expert in physical chemistry and the science of formulation, testified that a person of ordinary skill would understand that no method of measuring particle size is perfect: Every measurement of particle size has a standard deviation, also known as a coefficient of variation. JA 3867, 4120-4125, 4128. And so, according to both experts, a person of ordinary skill would read the "400 µm" figure with that deviation in mind. JA 3867, 4129-4130. Accordingly, that person would understand "400 µm" to mean "*about* 400 µm," just as the specification defines the term.

Indeed, Zydus's own actions indicate that a person of ordinary skill would construe the limitation in this way. Zydus's internal documents from 2007, for example, reveal that one of its strategies to avoid infringing the '994 patent was to prepare fine granules with an average particle diameter of *at least* 470 µm.

JA 4702. An internal email sent in 2008 by Pallavi Kharkar, a member of Zydus's intellectual property department, JA 2562-2563, also recognized that the "[l]imit of 400 or less can be extended beyond 400," JA 4722.[1] That same email suggested that the limit "might even go to 20% of 400 which is 480 microns." JA 4722. A PowerPoint that Zydus distributed internally in 2009 further acknowledged that a formulation containing fine granules with an average particle diameter of 409 µm fell within the scope of the patent. JA 4770; *see also* JA 2670-2671 (testimony of Pallavi Kharkar) (confirming this reading of the PowerPoint). As Dr. Byrn explained at trial, these documents demonstrate that Zydus itself understood that 400 µm was not a strict upper limit, even before the District Court issued its claim-construction opinion in this case. JA 4134-4138. Thus, the patent's specification, Dr. Bugay's and Dr. Byrn's expert testimony, and Zydus's own actions all lead to the same conclusion: that a person of ordinary skill would understand the upper limit of the average particle diameter of the fine granules to be "about 400 µm."

The question, then, is what qualifies as "about 400 µm." And in answering that question, a person of ordinary skill would naturally refer back to the deviation that accompanies any particle-size measurement: "About 400 µm" means 400 µm plus or minus the deviation. *See* JA 3867, 4129. A person of ordinary skill would

[1] Although the email referred to the doctrine of equivalents in stating that the limit could be extended, it is nevertheless probative of what a person of ordinary skill would understand the "400 µm" figure to mean. JA 4722.

also know that the deviation for particle-size measurements is generally understood to be ±10%. JA 4129 (testimony of Dr. Byrn) (explaining that a person of ordinary skill "would know that the number should be ten, ten percent, plus or minus ten percent"). After all, the U.S. Pharmacopeia, a national standard-setting body, states that for laser diffraction, the "coefficient of variation" for any measure of average particle size is "less than 10%." JA 301, 4312. An article published by the Product Quality Research Institute ("PQRI")—known as the "Snorek" article because of its lead author—reports the same figure. JA 8261. And Dr. Byrn testified that 10% is the accepted deviation not only for laser diffraction, but for "several other particle size methods, especially microscopy." JA 4133; *see also* JA 4150-4151.

Thus, to a person of ordinary skill in the art, "about 400 µm" means "400 µm (±10%)." The District Court was therefore correct to construe the limitation to incorporate a ±10% deviation. JA 67; *see also* JA 2550 (District Court explaining that the ±10% deviation does not "apply only to laser diffraction and only to batch/bulk sample measurements"). So construed, the limitation covers any tablet containing fine granules with an average particle diameter of up to 400 µm + 10%, or 440 µm. Indeed, as the District Court explained, because the limitation establishes an upper limit (i.e., "400 µm *or less*"), only the +10% matters; the –10% is encompassed within the "or less." JA 67.

In challenging this construction, Zydus does not dispute that the limitation should be read to incorporate *some* deviation. Rather, Zydus contends—as it did in the District Court, JA 1408-1409—that "[t]he proper construction for the claim term 'fine granules having an average particle diameter of 400 µm or less' is 'fine granules having an average particle diameter of precisely 400 µm or less,' using 'precisely' in its scientific meaning to include *small instrument errors*." Zydus Br. 47-48 (emphasis added). During *Markman* proceedings, Zydus explained that this meant that the limitation should be construed to "allow[] a variance in diameter of no more than ±3%." JA 1409. The dispute between the parties is therefore a narrow one: whether the deviation incorporated in the limitation should be ±10%, as the District Court concluded, or ±3%, as Zydus maintains.

Zydus's arguments in favor of a ±3% deviation do not withstand scrutiny. In the District Court, Zydus derived the ±3% figure from a different passage in the U.S. Pharmacopeia's chapter on laser diffraction that the court cited in support of the ±10% deviation. JA 1408. The passage on which Zydus relies concerns the procedure for "confirm[ing] the correct operation" of a laser diffraction instrument. JA 302, 4312. And the passage explains that if the instrument is working correctly, the variance when measuring "certified or standard reference material" will be "not more than 3%." JA 302, 4312.

Zydus's reliance on this passage is misplaced for two reasons. First, by its terms, the passage is addressed only to "confirm[ing] the correct operation of the *instrument*." JA 302, 4312 (emphasis added). And so, as Dr. Byrn explained at trial, the ±3% suggested in that passage refers only to *instrument* error. JA 4131 ("The three percent is the instrument error."); JA 4132 (agreeing that "the three percent applies only to instrument error"). The ±3% therefore does not reflect other variances associated with measuring particle size—such as the variance inherent in sampling. When, for example, granules are drawn from a tablet sampled from a batch, the average particle size of those granules will differ from the average particle size of the granules in other tablets from that batch, because, as Dr. Byrn explained, "no two tablets are exactly the same." JA 4122; *see also* JA 3723 (testimony of Dr. Bugay) ("Obviously there's going to be some variability there."). So, too, when granules are sampled from a vat before they are put in tablets, the average particle size of those granules may not necessarily be representative of the vat as a whole. JA 4123-4124. The ±3% also does not reflect the variance associated with the user—the person operating the instrument and measuring the particle size. Even the same user will not process a sample the same way twice: "There's always a little bit of difference," Dr. Byrn testified. JA 4123. Thus, as Dr. Byrn explained, "in real life, we have three factors that contribute to the deviation[:] the sample selection, the user and the instrument." JA 4122. The

±10% adopted by the District Court accounts for all three. JA 4125, 4129, 4131. The ±3% advocated by Zydus accounts for only one. Accordingly, the ±3% does not accurately capture the deviation associated with particle-size measurements.

Second, the instrument error that the ±3% addresses is defined in a particular circumstance: when measuring the size of "certified or standard reference material," designed for determining whether the instrument is working properly. JA 302, 4312. Certified reference material is regular in shape; the National Institute of Standards and Technology, for instance, manufactures such material in perfect spheres. JA 3979, 4119. The actual particles that pharmaceutical companies produce, however, are irregular in shape—as are Zydus's particles here. *See* JA 3979 (testimony of Zydus's expert, Dr. Harry Brittain) (acknowledging that the granules in Zydus's product are "irregularly-shaped spheres"). As a consequence, the variance in particle-size measurements will necessarily be more than ±3%. For, as even Zydus's experts acknowledged, the less spherical the particles are, the greater the variance will be. *See* JA 3983 (testimony of Dr. Brittain) ("The more you depart from true spherical, the further apart the results can be."); JA 4084 (testimony of Zydus's expert, Dr. Paula Meyer-Stout) ("The further you get away in your particle shape from that perfect sphericity, * * * the further these estimates get away from each other or that your diameters would differ.").

The reason for this increase in variance is simple. All methods of measuring particle size are indirect. *See* JA 3783 (testimony of Dr. Bugay) ("No particle size measurement does a direct three-dimensional assessment."); JA 3908 (testimony of Dr. Brittain) ("[A]ll particle sizing is somewhat indirect in nature."); JA 4083 (testimony of Dr. Meyer-Stout) ("The difficulty in this field * * * is that we really are trying to use one dimension, a diameter, to describe a three-dimensional geometry."). Each method takes a certain aspect of a particle, assumes that the particle is a perfect sphere, and then calculates what the diameter of that sphere would be, given that aspect. *See* JA 3981, 4083. Laser diffraction, for example, works by taking the pattern of diffraction caused by a particle, and calculating the diameter of a sphere with the same pattern. *See* JA 3607, 3737. Similarly, optical microscopy works by taking the cross-sectional area of a particle, and calculating the diameter of a sphere with the same area. *See* JA 3606, 3930, 3980. When a particle is irregularly shaped, however, it may not always hit the laser at the same angle, or have the same cross-sectional area under the optical microscope. *See* JA 3980 (testimony of Dr. Brittain) (discussing the "angular dependence of light scattering"); JA 3929 (testimony of Dr. Brittain) ("The microscope cannot tell the difference between an egg and a coin when viewed from above."). And this means that the same particle may not always be measured in the same way, even by the same instrument. This variability naturally increases the variance in particle-size

measurements. *See* JA 3982 (testimony of Dr. Brittain) (agreeing that "when applying any technique that reduces some experimental observable obtained on an irregular particle shape to that of an equivalent spherical particle, one must expect the introduction of [error]"). And although the ±3% deviation advocated by Zydus does not account for this increase, the ±10% deviation adopted by the District Court does. JA 301-302, 4312.

There is thus no basis for construing the limitation to incorporate only a ±3% deviation. A ±3% deviation reflects only—as Zydus puts it—"small instrument errors." Zydus Br. 48. It does not reflect the variance from sampling and user error, and it does not account for the additional variance from measuring irregularly shaped particles, as opposed to perfectly manufactured spheres. A person of ordinary skill would understand the limitation "400 µm or less" to incorporate the applicable deviation for particle-size measurements. And as the District Court concluded, the applicable deviation is ±10%, not ±3%.

None of Zydus's arguments undermines this conclusion. Zydus observes that two of the sources for the ±10% figure, the U.S. Pharmacopeia chapter and the Snorek article, were published in 2004 and 2007, respectively, after the 1999 filing date of the '994 patent. Zydus Br. 46. Dr. Byrn, however, testified that the ±10% figure was already "well understood" in the late 1990s, when the committees responsible for those publications were doing their work. JA 4132-4133; *see also*

JA 4130; *Energy Transp. Grp., Inc.* v. *William Demant Holding A/S*, 697 F.3d 1342, 1349 (Fed. Cir. 2012) (construing a claim term in light of an expert's testimony about what a person of ordinary skill in the art would have known at the time of the invention). Dr. Byrn was certainly in a position to know, because at the time he was the chair of the PQRI committee under which the Snorek committee worked. JA 4126. Zydus also contends that the U.S. Pharmacopeia reference relates only to errors from sampling fine granules from a "large vat." Zydus Br. 47. But that contention is not only contrary to Dr. Byrn's expert testimony, JA 4125, 4131, it finds no support in the U.S. Pharmacopeia itself, JA 301, 4312. Indeed, Zydus's only citation for that contention is a statement made by Zydus's own counsel during the *Markman* hearing. *See* Zydus Br. 47 (citing JA 1290-1291). Zydus also argues that the ±10% figure does not apply to measurements made through optical microscopy. *Id.* at 25. But as noted above, Dr. Byrn specifically testified that it does. JA 4133, 4150-4151.

Zydus's remaining arguments fail to show why its construction should be preferred over the District Court's. Zydus observes (at 45) that the '994 patent differentiates between "fine granules"—which in Claim 1 have an average particle diameter of "400 µm or less," JA 142—and "[c]onventional granules" —which have an average particle diameter of "400 µm or more," JA 124. But that shows merely that the line between "fine granules" and "conventional granules" is

400 µm, which Claim 1 already tells us. It does not establish how "400 µm" should be construed—let alone whether the applicable deviation is ±3% or ±10%.

Zydus also argues that the term "about," as used in the phrase "about 400 µm or less" in the specification, and the term "within," as used in the phrase "within 400 µm" in the file history, both connote "*downward* movement from 400 µm." Zydus Br. 46 (emphasis added). It is difficult, however, to square this argument with Zydus's own preferred construction, which allows for deviation in *both* directions for "small instrument errors" of ±3%. *Id.* at 48; *see also* JA 1409 (arguing, during *Markman* proceedings, that the limitation should be construed to "allow[] a variance in diameter of no more than ±3%"). Zydus's arguments fail in any event. For if "about" referred only to "downward movement," then the "or less" would be superfluous. And given that "within" is just another way of saying "or less," it is a mistake to read it as connoting anything more. The evidence on which Zydus relies does not resolve the question whether the limitation incorporates only "small instrument errors" of ±3%, as Zydus maintains, or a ±10% deviation, as the District Court concluded.

In short, the District Court's claim construction is correct. A person of ordinary skill would understand the limitation "400 µm or less" to incorporate a deviation. And it is well known in the art that the applicable deviation is ±10%.

B. The District Court's Finding Of Infringement Was Not Clearly Erroneous.

With the District Court's proper construction of Claim 1 in hand, the next step is the determination of infringement. "Infringement is a question of fact that, after a bench trial, [this Court] review[s] for clear error. Under the clear error standard, a reversal is permitted only when this court is left with a definite and firm conviction that the district court was in error." *Alza Corp.* v. *Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006) (citation omitted).

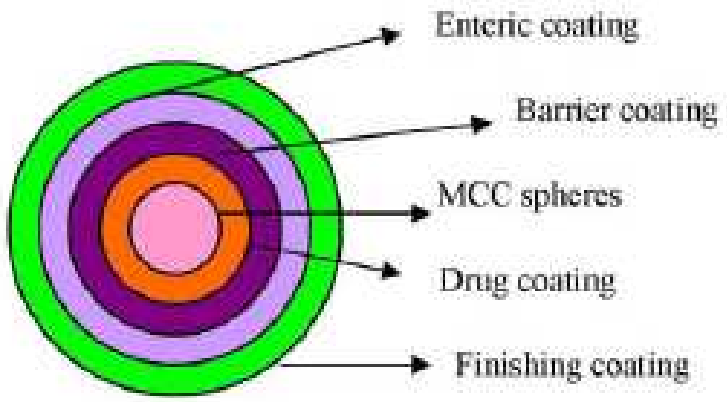
"An infringement inquiry provoked by an ANDA filing * * * is focused on the product that is likely to be sold following FDA approval." *Abbott Labs.* v. *TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002). "The proper inquiry * * * is whether, if a particular drug *were* put on the market, it *would* infringe the relevant patent." *Warner-Lambert Co.* v. *Apotex Corp.*, 316 F.3d 1348, 1366 (Fed. Cir. 2003) (internal quotation marks omitted).

Here, the District Court determined the average particle diameter of the fine granules in Zydus's ANDA product to be 420.46 µm—less than Claim 1's upper limit of 440 µm. JA 77-78. The court therefore found that if Zydus's ANDA product were put on the market, it would infringe the '994 patent. *Id.* The District Court's finding of infringement is not clearly erroneous.

1. A person of ordinary skill would treat each individual, coated core as a "fine granule," deagglomerating two or more cores stuck together before measuring particle size.

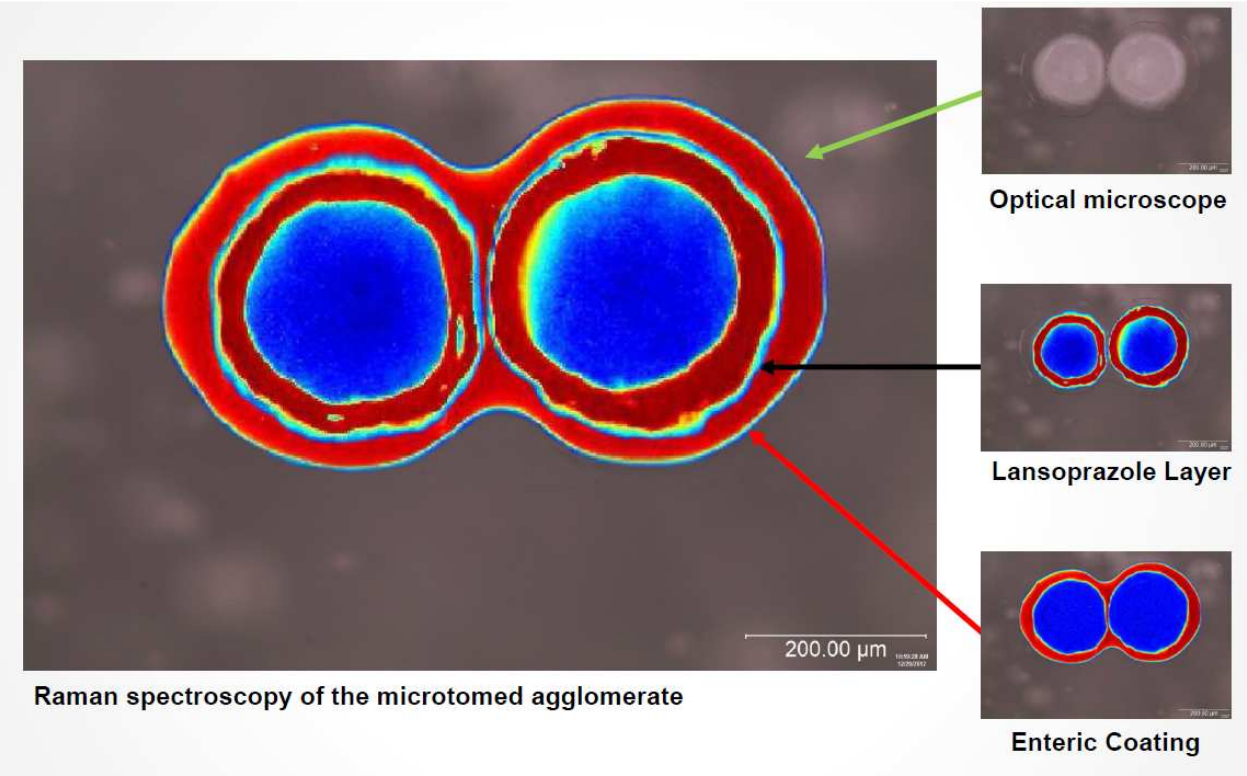
To begin, the District Court's finding rested on a proper determination of how a person of ordinary skill, in determining the average particle size of the "fine granules" in Zydus's ANDA product, would address the presence of individual, coated cores that are stuck together. JA 69.

The parties do not dispute that the following depicts a "fine granule":



JA 4635. This "fine granule"—which is actually a schematic taken from Zydus's ANDA submission—consists of a single spherical core, covered with various layers of coating, including a drug coating and an enteric coating. JA 3714-3715. There is no dispute that, for purposes of Claim 1, the diameter of this fine granule would be measured as the diameter of the core, plus all layers up to and including the enteric coating. JA 112, 3720-3721, 3914.

The goal of any pharmaceutical manufacturer is to produce individual, coated cores, as shown above. JA 3741-3742, 3904. But sometimes during the manufacturing process, two or more cores become stuck together, the enteric coat of one adhering to that of another. JA 3741, 3746-3748, 3904-3905. This is known as agglomeration:



JA 3603, 3745-3747.

Would a person of ordinary skill treat the agglomerate shown above as one "fine granule" or two? The District Court correctly concluded two, finding that a person of ordinary skill would know to make particle-size measurements of the two individual, coated cores, deagglomerating granules stuck together. JA 68-70.

As Dr. Bugay explained at trial: "To one skilled in the art, agglomerates is a well-known phenomenon and it is the objective of *any* particle size analysis to be measuring de-agglomerated, single entit[ies] * * * ." JA 3843 (emphasis added); *see also* JA 3743 (testimony of Dr. Bugay) ("[T]he goal of particle size determination is to measure individual particles."); JA 3882 (testimony of Dr. Bugay) (explaining that "one skilled in the art" tries "to achieve particle size determinations with individual entities, not agglomerated materials"). Thus, for example, the U.S. Pharmacopeia chapter on laser diffraction advises that "[i]f the presence of aggregates [another term for agglomerates] is suspected, this can be investigated using other techniques such as microscopy." JA 4309, 8240. Microscopy, after all, can detect the presence of agglomerates—and thus obtain a proper measure of particle size through deagglomeration—while laser diffraction cannot. JA 3742-3743. Even the user manual of the HELOS RODOS—a laser diffraction instrument referenced in the '994 patent, JA 126—expressly warns that "[s]ince [laser diffraction] is analyzing the dimensions of a cluster of adherent particles as one particle, it needs to be ensured the sample is free of agglomerates * * * before the analysis is performed." JA 4801; *see also* JA 4158 (testimony of Dr. Byrn) (explaining that the manual is "telling you to separate the agglomerates, get it free of agglomerates before you do the analysis"); JA 4148 (testimony of Dr. Byrn) (explaining that "many * * * laser diffraction units tell you to look at the

sample by microscopy"). In light of these authorities against measuring agglomerates as single particles, a person of ordinary skill in the art would hardly think she was required to do just that in the context of the '994 patent.

Treating each individual, coated core as a "fine granule" makes particular sense here, given that the goal of the manufacturing process is to avoid producing agglomerates altogether. As both sides' experts agreed, "ideally what you would like to make are individual particles that receive the coating." JA 3904 (Dr. Brittain); *see also* JA 3741 (testimony of Dr. Bugay) ("[T]he aim is to produce individual particles, individual granules."). That is because the pharmaceutical industry values a "consistent product" that "performs in a consistent manner," and when all of the coated entities are the same, there is "consistency [in] the administration" of lansoprazole. JA 3742, 3884 (testimony of Dr. Bugay). Because agglomerates undermine this consistency, they are undesirable. JA 3742, 3883-3884. Indeed, they are regarded as mistakes, caused by flaws in the manufacturing process—for instance, a coating process that is too long. JA 3884. It would thus make little sense to treat agglomerates as single entities under the patent. A person of ordinary skill would instead treat each coated core as what it was intended to be: an independent "fine granule."

That a person of ordinary skill would treat each individual, coated core as a "fine granule" finds further support in the patent's specification. There, a "granule"

is invariably described as consisting of a single, coated "core"—and never more than one. The specification, for example, speaks of "[*t*]*he* 'core'" as being "as uniform a sphere as possible, for reducing the irregularity of the coating." JA 131 (emphasis added). It explains that "a fine granule in the form of a rough sphere may be attained" because "the form of the powder is usually according to *the* core." *Id.* (emphasis added). And when the specification describes various methods for producing "fine granules," it does so under the heading "Production of Granules Having *a* Core." JA 133-137, 139-141 (emphasis added). Indeed, the phrase "granules having *a* core" appears no fewer than 89 times throughout the specification. JA 124, 133-142 (emphasis added). Thus, as Dr. Bugay testified at trial, the specification teaches that *each* coated core is a "fine granule." JA 3719-3720. "Nowhere," as the District Court concluded, "does the '994 patent teach that a 'fine granule' can be built from more than one spherical core." JA 69.

In light of the foregoing, the District Court was correct to conclude that a person of ordinary skill would treat each individual, coated core as a "fine granule," regardless of whether two or more coated cores were stuck together. *Id.* As the District Court explained, a person of ordinary skill would "know[] to deagglomerate prior to subjecting the sample to particle size measurement." *Id.*

Zydus resists this conclusion, arguing that the '994 patent does not discuss deagglomeration. Zydus Br. 49. Instead, Zydus contends, the inventors

themselves used laser diffraction for measuring particle size and regarded it as the "best mode" for doing so. *Id.* at 10, 49-50. Based on the fact that laser diffraction cannot detect the presence of agglomerates, Zydus concludes that the inventors must have intended agglomerates to be measured as single particles.

The fact that the '994 patent does not discuss deagglomeration, however, is easy to explain: The inventors presumed that their batches would include only a *nominal* amount of agglomerates. *See* JA 3741, 3794, 3852, 3883, 3904. When the number of agglomerates is nominal, using laser diffraction is perfectly appropriate and perhaps even the "best mode." JA 132-133 ('994 patent); JA 3744 (testimony of Dr. Bugay) ("If we're talking nominal meaning very, very small amounts of agglomerates, then yeah, one could justify laser diffraction if we're working with very low numbers."). But that is only because there are so few agglomerates that it does not matter how they are measured; it says nothing about how agglomerates should be measured when they reach a critical mass. Indeed, the patent specification refers to laser diffraction as only one "example" of a method for measuring particle size. JA 126. Thus, although the inventors may have had no need to deagglomerate their own batches, that does not mean that they considered agglomerates to be "fine granules" in the context of the patent.

Zydus protests that there is no evidence of what a "nominal" amount of agglomerates means. Zydus Br. 49. But Zydus's own expert in pharmaceutical

chemistry and industrial pharmacy, Dr. Paula Meyer-Stout, suggested that "nominal" meant any factor that did not affect whether a batch infringed the patent. JA 4071, 4097, 4108. So under that definition, a "nominal" amount of agglomerates is any amount that would not affect whether the average particle diameter measures 440 µm or less.

Zydus also contends that there is no evidence that "exemplary batches" of the '994 patent would have only a nominal amount of agglomerates. Zydus Br. 50. But as noted above, both sides' experts testified that the ideal number of agglomerates is zero. According to Dr. Bugay, the goal of any manufacturing process is "to minimize, if not eliminate," the number of agglomerates. JA 3794; *see also* JA 3741-3742, 3852 (testimony of Dr. Bugay). He said it is "desirable" and "expected" to "have as little agglomeration as possible." JA 3883. Zydus's expert in physical chemistry and the science of formulation, Dr. Harry Brittain, agreed; he testified that "ideally" a manufacturer would produce individual particles. JA 3894-3895, 3904. Thus, the evidence amply demonstrates that an exemplary batch would have only a nominal amount of agglomerates. And that is why the inventors saw no need to discuss deagglomeration in their patent.

Finally, Zydus observes that the purpose of having "fine granules" of a certain size is so that they do not "impart roughness in the mouth." JA 123. From this, Zydus infers that what matters is the diameter of the agglomerate as a whole,

not the diameter of its component, coated cores. Zydus Br. 51-52. But as the District Court noted, the avoidance of roughness in the mouth is not itself a limitation in Claim 1 of the patent. JA 63. Moreover, the fact that the inventors sought to avoid roughness in the mouth explains only why they insisted on "an average particle diameter of 400 µm or less." It does not resolve what they meant by "fine granules," particularly given the evidence above. That evidence shows that a person of ordinary skill would understand "fine granules" to consist of a single core, and would thus deagglomerate before measuring particle size. The District Court's determination that a person of ordinary skill would "know[] to deagglomerate prior to subjecting the sample to particle size measurement" is not clearly erroneous. JA 69.[2]

2. Particle-size testing showed that the individual, coated cores of Zydus's ANDA product have an average particle diameter of less than 440 µm.

The District Court's finding of infringement also rested on the only evidence of particle-size testing of the individual, coated granules in Zydus's ANDA product in the case—testing conducted by Dr. Bugay, Takeda's expert in pharmaceutical formulation. In performing that testing, Dr. Bugay followed techniques well known to a person of ordinary skill in the art.

[2] Zydus concedes that the issue of whether a person of ordinary skill would deagglomerate is an issue of infringement, subject to clear-error review. *See* Zydus Br. 49, 53.

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First, Dr. Bugay took three tablets from a batch of product Zydus manufactured in 2012. There is no dispute that the 2012 batch reflects the product Zydus would likely sell . JA 79, 2772, 3721-3722, 3763-3765. And there is no dispute that the three tablets Dr. Bugay sampled were representative of Zydus's product. JA 3723.

Next, Dr. Bugay extracted the pellets from each tablet using a "very simple" procedure. JA 3723-3724. Each tablet was placed into a flask containing a water-based solution with a pH of 4.5. JA 3724-3725. That solution dissolved the tablets and the outermost coating of Zydus's pellets, leaving behind the pellets with their enteric coating intact. JA 3725, 3729.

Dr. Bugay then examined Zydus's enteric-coated pellets using optical microscopy, a "standard" technique, JA 3976, "widely recognized within the pharmaceutical industry," JA 3738. Optical microscopy allowed Dr. Bugay to view actual images of the pellets using a software program called ExpertShape. JA 3743, 3749-3751. In doing so, Dr. Bugay found that over 80% of the pellets were non-agglomerated, individually coated cores, about 18% were made up of two enteric-coated cores stuck together, and the remaining percentage consisted of three or more enteric-coated cores stuck together. JA 3758-3759. Using a "standard" feature of the software, Dr. Bugay instructed the program to measure each agglomerate as two or more fine granules instead of one. JA 3749-3751.

Indeed, by positioning a ruler on each image, he was able to mark precisely where the deagglomeration was to occur. JA 3750. After deagglomerating, Dr. Bugay found that the average particle diameter of the "fine granules" in each tablet was 413.76 µm, 426.94 µm, and 416.24 µm. JA 3752. These figures average to 418.98 µm per tablet. *Id.*

Finally, Dr. Bugay conservatively adjusted his calculations upward to account for granules potentially lost during the testing process. That adjustment was based on the amount of lansoprazole found in the solution used to dissolve the tablets; in the case of each tablet, Dr. Bugay detected the presence of 1% or less lansoprazole in the filtrate. JA 3753. Based on the amount of lansoprazole detected, Dr. Bugay calculated the number of granules that had been potentially lost. *Id.* He then assumed, conservatively, that each of those granules was equivalent to the largest subset of granules found in each tablet, and added those particle-size diameters to the rest of his measurements. JA 3754. In light of these adjustments, Dr. Bugay determined the average particle diameter of the fine granules in Zydus's ANDA product to be 420.46 µm—the figure the District Court ultimately adopted. JA 77-78, 3755.

Zydus challenges the District Court's reliance on Dr. Bugay's testing on several grounds. Zydus first contends that Dr. Bugay dissected agglomerates in a subjective manner. Zydus Br. 28, 40. Dr. Bugay's use of Raman spectroscopy,

however, demonstrates otherwise. Raman spectroscopy is a technique for identifying the different chemical compositions in a particle. JA 3745-3746. And here, Raman spectroscopy showed that the agglomerates among Zydus's particles were indeed what Dr. Bugay suspected them to be: the adhering together of multiple enteric-coated cores. JA 3746-3748. Consider, for example, the figure shown above on p. 28, which is one of the images Dr. Bugay generated using Raman spectroscopy. It shows clearly that the particle under examination is not a granule with an odd shape, but two granules whose enteric coats have become stuck together. As the District Court observed, "Dr. Bugay confirmed via Raman spectroscopy that agglomerates in Zydus's ANDA product were comprised of component, individual enteric-coated entities." JA 73. Thus, the deagglomeration performed by Dr. Bugay was far from subjective.

Moreover, there is no evidence that any subjectivity in *how* the agglomerates in Zydus's ANDA product were dissected had any impact on the average particle size of the "fine granules." Virtually all of the agglomerates in Zydus's product (approximately 18% of Zydus's pellets) consisted of only two individual, coated cores stuck together. JA 3759. How those agglomerates were divided in two could have no impact on the average particle size of the "fine granules." As for Zydus's cherry-picked example of a high-order agglomerate, *see* Zydus Br. 29, only 0.5% of Zydus's 15,000 pellets consisted of more than three granules stuck

together. JA 3759. Given how few of those high-order agglomerates there were, any subjectivity in how those agglomerates were dissected had no effect on the ultimate finding of infringement.

Zydus next contends that Dr. Bugay's deagglomeration of granules that were physically adhered together violated the constraints of the ExpertShape software, which, according to Zydus, is supposed to be used only to deagglomerate particles that are "touching." Zydus Br. 27. Dr. Bugay, however, described his use of the software as "standard routine." JA 3749. And indeed, the section of the ExpertShape manual he followed is entitled "How to separate several particles stuck together." JA 3749-3750, 8187. There was thus nothing exceptional about Dr. Bugay's use of the software to deagglomerate Zydus's granules.

Zydus also points to an instance in which it believes Dr. Bugay removed an agglomerate entirely from calculation. Zydus Br. 29. There is no evidence, however, that this occurred more than once out of the approximately 15,000 pellets Dr. Bugay examined. JA 3723, 3758-3759, 3986. Nor is there any evidence that omitting this one agglomerate had any impact on the ultimate finding of infringement. After all, as Zydus's own expert acknowledged, even if the agglomerate had been included in the calculation, it would have been counted as several individual granules, not a single particle. JA 3939. So including it would

have had a nominal effect on the average particle diameter of the fine granules in the tablet—and could have even lowered the average.

Finally, Zydus contends that Dr. Bugay's calculation of average particle diameter could be off by as much as 10%, given the deviation recognized by the District Court. Zydus Br. 51. The District Court's claim construction, however, already accounts for this deviation, by holding that any measurement within 10% of 400 µm is "about 400 µm." And because Dr. Bugay's 420.46-µm figure is "about 400 µm," that is the end of the inquiry; the deviation need not be taken into account a second time.

In sum, Zydus's challenges to Dr. Bugay's testing fail. Substantial evidence supports the District Court's finding that the average particle diameter of the fine granules in Zydus's ANDA product is 420.46 µm. Accordingly, the District Court did not clearly err in finding that Zydus's ANDA product would infringe Claim 1.

C. The Does Not Resolve The Infringement Inquiry.

The District Court was also correct to conclude that Zydus's

does not resolve the infringement inquiry. JA 78-81. An ANDA specification controls when it "defin[es] a proposed generic drug in a manner that directly addresses the issue of infringement." *Abbott Labs.*, 300 F.3d at 1373. That is not the case here.

CONFIDENTIAL MATERIAL OMITTED

Zydus

JA 4551 (capitalization and boldface removed). But, in testing a batch of Zydus's product that a senior director at Zydus testified with the , JA 79, 2772, 3721-3722, 3763-3765, Dr. Bugay found that the average particle diameter of Zydus's fine granules was less than the upper limit established by Claim 1, JA 3730. Dr. Bugay's testing is conclusive proof that the does not resolve the issue of infringement.

Even if there were no actual testing, it would be clear from the terms of the that the ANDA is not dispositive. That is so for two reasons. First, as the District Court observed, Zydus's does not require deagglomeration in determining average particle diameter. JA 80. Instead, the , a laser diffraction instrument that is incapable of deagglomeration. JA 3762, 3765, 3767, 4551. Thus, when the

JA 4551 (capitalization and boldface removed), that figure includes agglomerates measured as single particles, JA 3767, 3770-3771. Agglomerates, however, are not measured the same way under Claim 1, as the District Court found. Under Claim 1,

agglomerates are measured as the individual, coated entities they comprise. And so Zydus's ANDA product could contain

, but "fine granules" having an average particle diameter of *less* than 440 µm when measured under Claim 1. Therefore, as Zydus has expressly conceded, the

does not resolve the issue of infringement if the court's determination is correct. JA 80 (District Court noting Zydus's concession at trial); JA 4260-4261 (Zydus's counsel stating at trial that

, okay. * * * Therefore, it would not be dispositive of the issue of infringement if you say that we should not have been * * * tak[ing] them into account."); Zydus Br. 53 (arguing that Zydus's ANDA resolves the issue of infringement only "[*a*]*bsent* the district court's clearly erroneous underlying finding[]" that "hard agglomerates must be deagglomerated" (emphasis added)).

Second, as the District Court also noted, Zydus's does not require proper representative sampling of granules for testing. JA 80. According to Zydus's own expert, Dr. Brittain, it is the "general consensus" that only a method known as dynamic sampling—which draws granules while they are in motion—"can yield the desired representative sample" of pre-tableted granules. JA 3998. Zydus, however, uses a method known as static sampling, which draws

granules while they are stationary, before they are put into tablets. JA 3767-3768, 3773. Static sampling may result in a higher measure of average particle diameter, because smaller particles tend to segregate to the bottom of the heap, where they have less of a chance of being drawn. JA 3768. The upshot is that a batch of Zydus's product could comply with the when tested using static sampling, but infringe the '994 patent when tested using dynamic sampling. For this reason as well, the does not resolve the issue of infringement. Indeed, Zydus acknowledges that its is not dispositive if static sampling is improper. Zydus Br. 53 (arguing that Zydus's ANDA resolves the issue of infringement only "[*a*]*bsent* the district court's clearly erroneous underlying finding[]" that static sampling "does not provide a representative sample of granules" (emphasis added)).

This Court's decision in *Bayer AG* v. *Elan Pharmaceutical Research Corp.*, 212 F.3d 1241 (Fed. Cir. 2000) ("*Elan*"), is not to the contrary. *Elan* involved a patent of Bayer's claiming a drug containing nifedipine crystals of a specific surface area, up to 4 m^2/g. *Id.* at 1246. After Elan filed an ANDA, Bayer sued for infringement. *Id.* Elan then amended its ANDA to specify a specific surface area of 5 m^2/g or greater—beyond the limit of the patent. *Id.* This Court subsequently affirmed the grant of summary judgment for Elan, concluding that "the specification in Elan's ANDA defines its product in a way that directly addresses

the question of infringement—the [specific surface area] of the nifedipine crystals." *Id.* at 1248-49. Indeed, Bayer did not have any evidence that *if* Elan complied with the amended ANDA, it could infringe the patent. *See id.* at 1249-50.

Here, by contrast, the record shows that regardless of whether Zydus complies with the based on its faulty testing methodology, it would infringe the patent nonetheless. Thus, as the District Court concluded, this case is more like *Bayer AG* v. *Biovail Corp.*, 279 F.3d 1340 (Fed. Cir. 2002) ("*Biovail*"). That case, decided two years after *Elan*, involved the same patent and a "nearly identical" ANDA as in *Elan*. *Id.* at 1346. Defending against Bayer's infringement action, Elan contended that Bayer was collaterally estopped from claiming infringement because, just as in *Elan*, the ANDA specified a nifedipine-crystal surface area of 5 m^2/g or greater. *See id.* at 1343, 1346. But this Court held that *Elan* was not controlling, because Bayer had introduced evidence in the second case that Elan's product could be made in strict conformity with the ANDA and nevertheless infringe the patent. *Id.* at 1346-47. That evidence included actual testing of Elan's product, showing that it infringed. *Id.* Accordingly, the ANDA did not resolve the question of infringement.

Just so here. Although Zydus

does not require deagglomeration or representative sampling. As a result,

the does not resolve the issue of infringement—a conclusion confirmed, as in *Biovail*, by actual testing of Zydus's product. That testing showed that Zydus's product could have , but "fine granules" with an average particle diameter of less than 440 µm within the scope of the patent—in other words, just as in *Biovail*, Zydus could comply with the (based on its own faulty testing methodology) and still infringe the patent. Accordingly, the is not controlling, and the District Court's finding of infringement should be affirmed.

II. THE DISTRICT COURT CORRECTLY HELD THAT ZYDUS DID NOT PRESENT CLEAR AND CONVINCING EVIDENCE THAT THE PATENT IS INVALID.

"A patent shall be presumed valid," and the "burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity." 35 U.S.C. § 282. That party must prove the invalidity of the patent by clear and convincing evidence. *Microsoft Corp.* v. *i4i Ltd. P'ship*, 131 S. Ct. 2238, 2242 (2011).

Zydus did not meet its burden here. The District Court was therefore correct to hold that Claim 1 is not invalid.

A. The District Court Correctly Concluded That Claim 1 Is Not Invalid For Lack Of Enablement.

Zydus contends that Claim 1 is invalid for lack of enablement. Title 35 U.S.C. § 112(a) requires a specification to "contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same." "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *MagSil Corp.* v. *Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012) (internal quotation marks omitted). "Enablement is a question of law that [this Court] review[s] without deference, based on underlying factual inquiries that [this Court] review[s] for clear error." *Cephalon, Inc.* v. *Watson Pharms., Inc.*, 707 F.3d 1330, 1336 (Fed. Cir. 2013).

Zydus argues that Claim 1 does not enable one skilled in the art to practice the invention for three reasons. First, Zydus contends that Claim 1 is not enabling because, as construed by the District Court, the claim results in a mathematical impossibility. Zydus Br. 56-59. According to Zydus, the patent specifies a maximum particle diameter of "practically 425 µm or less," where "practically" is defined as allowing for a "small quantity" of particles above the maximum. JA 126, 142. Under Claim 1, however, the particles may have an "average particle

diameter" of 440 µm, where "average particle diameter" is defined as the "median diameter." JA 126. Thus, Zydus contends that the court's claim construction "creates the mathematical impossibility where the median of a *given set* is above the stated maximum." Zydus Br. 58 (emphasis added).

That *would* be impossible—if both the maximum and the median pertained to the same "*given set*." But they do not. In Claim 1, the patent claims a set of particles whose median particle diameter is 440 µm or less. JA 142. In Claim 7—a separate claim—the patent claims a different set of particles whose maximum particle diameter is practically 425 µm or less. *Id.* Though the sets of particles claimed by the two claims may overlap, nowhere does the patent require that a given set satisfy both at the same time. That Claims 1 and 7 spell out two independent concepts is confirmed not only by the patent specification—which treats the maximum as a limitation "[*a*]*side* from" the median, JA 126 (emphasis added)—but also by the testimony of both sides' experts, Dr. Bugay and Dr. Brittain—who understood them to be distinct concepts as well, JA 89-90, 3920-3921, 4140-4143. A person of ordinary skill would thus not find it impossible to practice Claim 1.

Zydus next contends that Claim 1 is not enabling because, as construed by the District Court, the claim encompasses not just "fine granules," but also "conventional granules." Zydus Br. 42, 57. The patent distinguishes "fine

granules" from "conventional granules," and describes the latter as "having a large particle diameter (400 µm or more of average particle diameter)." JA 124. Zydus contends that there is no "essence" to the invention if Claim 1 is construed to cover granules having an average particle diameter larger than 400 µm. Zydus Br. 42. The patent, however, treats "fine granules" and "conventional granules" as simply two sides of the same line: "Fine granules" have an average particle diameter of "400 µm or less," while "conventional granules" have an average particle diameter of "400 µm or more." Accepting, then, that "400 µm or less" is properly construed to mean "440 µm or less," it follows that conventional granules have an average particle diameter of 440 µm or more. And indeed, Dr. Byrn testified that he would view conventional granules in precisely that way. *See* JA 4145 ("Conventional granules are bigger than 440 microns * * * ."). Thus, even as construed by the District Court, Claim 1 does not capture "conventional granules."

Third and finally, Zydus contends that Claim 1 is not enabling because the patent "leaves open the possibility of the use of a number of known techniques for the determination of average particle diameter." Zydus Br. 42, 62-63. According to Zydus, each of these techniques could yield a different value, so a person could never tell if she was practicing the invention or not.

Zydus is wrong. To begin, the universe of possible techniques for measuring particle size is not as limitless as Zydus makes it out to be. After all, the

patent itself references laser diffraction as an "example" of a method for measuring particle size. JA 126. And the authorities on laser diffraction, in turn, reference optical microscopy as the preferred method when agglomerates are "suspected." JA 4309, 8240 (U.S. Pharmacopeia); *see also* JA 4148 (testimony of Dr. Byrn) (explaining that "many * * * laser diffraction units tell you to look at the sample by microscopy"). So from the very outset, a person of ordinary skill would be directed to two "widely recognized" techniques in the pharmaceutical industry. JA 3738. And that person would further be told exactly when to use each one: laser diffraction when there are no (or nominal) agglomerates, and optical microscopy when there are many. JA 3744. There would be no undue experimentation in determining the proper method here.[3]

Zydus suggests the possibility of a third option, the so-called "Coulter counter" method. Zydus Br. 63. That method involves sending particles through a current, measuring the length of the interruption, and calculating the diameter of a sphere that would have caused the same interruption. JA 4072. Zydus's expert, Dr. Meyer-Stout, testified that she was "not sure it's possible to design an accurate and sensitive Coulter counter methodology for these particles." JA 4087. And that is because, in Dr. Meyer-Stout's view, using the Coulter counter method would risk

[3] Zydus does not dispute that one skilled in the art would know how to measure particle size using laser diffraction or optical microscopy. Indeed, Zydus's internal documents show that Zydus measured particle size using laser diffraction without undue experimentation. JA 4734, 4741, 4780.

rupturing the enteric coating of the granules and skewing the particle-size distribution. *Id.* But as the District Court found, Zydus "did not offer any more specific evidence of the amount of experimentation necessary to use a Coulter counter instrument or of past failed efforts to use a Coulter counter instrument to measure the average particle diameter of fine granules in an ODT of the '994 patent." JA 86. Moreover, "the enablement requirement is met if the description enables *any* mode of making and using the invention." *John Hopkins Univ.* v. *CellPro, Inc.*, 152 F.3d 1342, 1361 (Fed. Cir. 1998) (emphasis added) (internal quotation marks omitted). Thus, whether the Coulter counter method could be used without undue experimentation is irrelevant, because a person of ordinary skill would be able to practice the invention using laser diffraction and optical microscopy.

Of course, as Zydus points out, laser diffraction and optical microscopy may yield measurements that are different. But the ±10% deviation incorporated into the claim construction already accounts for that variability. As Dr. Byrn testified, the ±10% reflects not only the variance in measurements while using one technique, but also the variance in measurements while "switch[ing] between technique[s]." JA 4151. So the fact each technique could yield a different value does not invalidate the patent. As both sides' experts agreed, each technique is "correct," though the values they give may not be exactly the same. JA 3739 (testimony of

Dr. Bugay); *see also* JA 3983 (testimony of Dr. Brittain) (acknowledging that he had published several articles stating that "the correct but differing particle size results obtained using various instruments are all equally correct"); JA 4086 (testimony of Dr. Meyer-Stout) ("[N]either method is incorrect if used correctly, but they give different values."); JA 4121 (testimony of Dr. Byrn) ("Each method is correct in its own way."). And though those values may differ, a person skilled in the art would regard them as "equivalent" after taking into account the standard deviation. JA 3738 (testimony of Dr. Bugay) ("No, [laser diffraction and optical microscopy] wouldn't give precisely exactly the same numbers, but they will give equivalent numbers with respect to any varian[ce] associated with either technique."). That person, using laser diffraction or optical microscopy, would thus be able to practice the invention without undue experimentation.

Zydus cites, for the first time on appeal, *Amgen Inc.* v. *Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003), and *Honeywell Int'l, Inc.* v. *ITC*, 341 F.3d 1332 (Fed. Cir. 2003), but both cases are far afield. Neither case held that a patent was invalid for lack of enablement; rather, the issue in both cases was whether a patent was invalid as indefinite. *See Amgen*, 314 F.3d at 1342; *Honeywell*, 341 F.3d at 1334. Thus, their holdings have no application here. In any event, the patents in *Amgen* and *Honeywell* were indefinite because a person of ordinary skill would not know the correct standard to use for conducting an

analysis. *See Amgen*, 314 F.3d at 1341-42; *Honeywell*, 341 F.3d at 1339-40. There is no such problem here. In this case, the evidence showed that each of the methods for measuring particle size is correct, and that all will yield "equivalent" results. JA 3738 (testimony of Dr. Bugay). Accordingly, a person of ordinary skill could practice the invention without undue experimentation. And because Zydus did not present clear and convincing evidence to the contrary, the District Court correctly held that Zydus did not meet its burden of proving that the patent is invalid for lack of enablement.

B. The District Court Did Not Clearly Err In Finding The Written Description Requirement Satisfied.

Zydus also contends that Claim 1 is invalid for lack of a written description. Title 35 U.S.C. § 112(a) contains a written description requirement separate from enablement. *Ariad Pharms., Inc.* v. *Eli Lilly & Co.*, 598 F.3d 1336, 1340 (Fed. Cir. 2010) (en banc). "The purpose of the written description requirement is to ensure adequate disclosure of the invention. A specification adequately describes an invention when it reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Pozen Inc.* v. *Par Pharm., Inc.*, 696 F.3d 1151, 1166 (Fed. Cir. 2012) (internal quotation marks and citation omitted). Whether the patent satisfies the written description requirement is a question of fact reviewed for clear error. *Id.*

According to Zydus, the patent here lacks an adequate written description because it does not explain the effect of compression forces on the average particle diameter of the fine granules. Zydus Br. 59-60. The fine granules are subjected to such forces during the manufacturing process, when they are compressed with other materials to form tablets. JA 4088-4089. Zydus argues that the patent fails to inform a person of ordinary skill how to ensure that these forces do not alter the size of the fine granules during tableting. As a consequence, Zydus contends, the fine granules may be found to be infringing or not, depending on whether they are measured before tableting or after.

A patent can be deficient for failing to describe the effect of compression forces, however, only if there is such an effect to describe. Here, the evidence shows that there is none. Dr. Bugay tested over 18,000 granules from Zydus's tablets, all of which had undergone compression forces during the tableting process. JA 3723. If those forces had affected the size of the granules, there would have been indications. But Dr. Bugay did not observe any cracking in the structure of the granules, JA 3757, 3873; in fact, he reported that they had retained their "general spheroidal shape," JA 3873. His Raman spectroscopy, moreover, revealed no disruption in the granules' enteric coating. JA 3748, 3757, 3872. And the fact that only 1% of lansoprazole was detected in the solution used to dissolve the tablets—a "minimum amount of leakage," as Dr. Byrn put it—indicated further

that "the granules weren't damaged." JA 4165; *see also* JA 3757, 3872 (testimony of Dr. Bugay). In short, none of the telltale signs of damage from compression was present—no cracking, no deformation, no disruption, no leakage. Therefore, Dr. Bugay concluded, compression forces had no impact on the granules during tableting. JA 3756-3757.

That there was no evidence of effects from compression is no surprise. After all, the level of compression used in making these tablets is not high to begin with. That is because these tablets are supposed to disintegrate in the mouth. JA 4162. If the compression forces used to make them are too high, then the resulting tablets will be packed too tightly to be able to disintegrate quickly enough. JA 4162, 4167-4168. So, in the words of Dr. Byrn, "[i]t's just not common sense" to expose the granules to compression forces so high that the granules could be affected. JA 4162. If a manufacturer did that, it would defeat the purpose of making an orally disintegrating tablet in the first place. The enteric coating of Claim 1, moreover, is specifically designed to protect the granules from damage, including during compression. JA 4163-4164. So when the granules are exposed to compression forces, the granules are not altered.

Against all this, Zydus offers only speculation about the effect of compression forces. It points, for example, to the testimony of Dr. Meyer-Stout, who opined that compression forces might affect the granules. JA 4089-4090. But

she could not say what overall effect those forces would have on average particle diameter; indeed, she "couldn't predict" whether the average would even go up or down. JA 4092. Zydus also points to the testimony of Dr. Byrn. But all he said was that it was "*technically* * * * possible" for the average particle diameter of the granules to go from non-infringing to infringing during tableting. JA 4189 (emphasis added). He also stated that such an occurrence would be "rare," JA 4189, and disagreed with any suggestion that compression forces would "affect [the granules] significantly," JA 4162. The District Court did not clearly err in finding that Zydus did not present clear and convincing evidence that the patent is invalid for lack of written description. JA 98.

Zydus cites *Eli Lilly & Co.* v. *Teva Pharmaceuticals USA, Inc.*, 619 F.3d 1329 (Fed. Cir. 2010), but its reliance on that decision is misplaced. At issue in *Eli Lilly* were patents that claimed particles of a certain size. *Id.* at 1344. The patents were construed to impose that limitation both before and after tableting. *Id.* The evidence showed, however, that the tableting process affected particle size; indeed, Eli Lilly presented actual testing showing that Teva's particles fell *outside* the range claimed by the patents when measured before tableting, but *within* that range when measured after. *Id.* In light of that evidence, the district court held the patents invalid for failure to meet the written description requirement. *Id.* The court noted that the patents did not mention the idea of measuring the particles

after tableting, or give any indication that post-tableting measurements could be relevant. *Id.* at 1344-45. On that record, this Court affirmed, emphasizing that the question on appeal was limited to whether the district court's finding was "clearly erroneous." *Id.* at 1345. Although the record contained "conflicting evidence" about how a person of ordinary skill would read the patents, the Court could not say that the district court had clearly erred. *Id.*

There are likewise no grounds for overturning the District Court's finding here. In *Eli Lilly*, actual testing showed that the tableting process affected particle size. In this case, the evidence is just the opposite: Actual testing, conducted by Dr. Bugay, showed no effect from compression forces on the average particle diameter of Zydus's granules. And that was the only actual testing on the subject. Indeed, as the District Court observed, "Zydus offered no test results evidencing that compression forces would impact particle size." JA 94. Thus, unlike in *Eli Lilly*, there was no need for the patent to discuss the notion of measuring granules post-tableting, or describe the effects of the tableting process on particle size. Accordingly, the District Court was justified in finding that Zydus fell short of presenting clear and convincing evidence of a lack of written description. And given that the standard of review here is the same deferential standard as in *Eli Lilly*, the outcome here should be the same, too: The District Court should be affirmed.

In any event, even if Zydus had presented clear and convincing evidence that compression forces affect the granules, the patent would still satisfy the written description requirement. There is, after all, no dispute that a person of ordinary skill would know how to extract granules from a finished tablet to measure their size. *Cf. Eli Lilly*, 619 F.3d at 1344-45 (noting the district court's conclusion that, "after reading the patent, a person of ordinary skill would *not* understand how to extract [the] particles from a formulation in order to determine whether they fall within the claimed particle size range" (emphasis added) (internal quotation marks omitted)). Doing so, according to Dr. Bugay, would require no special training or education beyond that of a person of ordinary skill. *See* JA 4169 ("[A] technician could do the extraction quite easily."). In fact, Zydus itself had no problem extracting granules from finished tablets for particle-size testing while developing its ANDA product. *See* JA 97, 2843-2844, 4169-4171, 4734. So even if compression forces did have an effect during tableting, a person of ordinary skill could simply measure the size of the particles after tableting to account for the effect. For this reason, too, there was no need for the patent to describe the effect of compression forces. The District Court did not clearly err in finding the written description requirement satisfied.

C. The District Court Correctly Concluded That Claim 1 Is Not Indefinite.

Finally, Zydus contends that Claim 1 is invalid for indefiniteness. The requirement of definiteness is set forth in 35 U.S.C. § 112(b), which provides that a patent must contain "claims particularly pointing out and distinctly claiming the subject matter which the inventor * * * regards as the invention." To prove that a claim is indefinite, "an accused infringer must * * * demonstrate by clear and convincing evidence that one skilled in the relevant art could not discern the boundaries of the claim based on the claim language, the specification, the prosecution history, and the knowledge in the relevant art." *Wellman, Inc.* v. *Eastman Chem. Co.*, 642 F.3d 1355, 1366 (Fed. Cir. 2011). Whether a claim is indefinite is a question of law reviewed de novo. *See id.* at 1365.

Zydus argues that incorporating a ±10% deviation into the limitation "400 µm or less" renders Claim 1 indefinite. Zydus Br. 38, 43, 55-56. According to Zydus's expert, Dr. Brittain, the deviation results in an upper limit "somewhere between 360 and 440 microns." JA 3966. And so, Zydus contends, a person of ordinary skill is left to guess where the line between infringement and non-infringement lies.

Zydus, however, misunderstands the effect of the deviation. The deviation does not blur the line between infringement and non-infringement; it *clarifies* it. The patent specifies that any average particle diameter of "about 400 µm" or less is

infringing. JA 126; *see also supra* pp. 14-17. That is the line between infringement and non-infringement: "about 400 µm." The deviation does not move that line. It simply clarifies what "about 400 µm" means: anything from 360 µm to 440 µm. And because all of those values are "about 400," all of them are infringing: 440 µm is infringing, as is 439 µm, as is 438 µm, and so on.

A person of ordinary skill would therefore understand that 440 µm is the upper limit established by Claim 1. 440 µm is "about 400 µm," and the claim covers any average particle diameter of "about 400 µm" or less. So any average particle diameter of 440 µm or less falls within the claim. The fact that any value between 360 µm and 440 µm is also "about 400 µm" does not matter, because, as Dr. Bugay explained, all of those values are already "encompassed by the upper threshold of 440 microns." JA 3719; *see also* JA 3865 (testimony of Dr. Bugay) ("[The 440] gives the upper threshold that also encompasses the negative ten percent."). Thus, in the words of Dr. Byrn, "when you read the patent, you go from 440 and 360 becomes redundant." JA 4118; *see also* JA 4146 (testimony of Dr. Byrn) ("It's redundant."). A person of ordinary skill would simply disregard the –10% and pay attention only to the +10%. *See* JA 3719 (testimony of Dr. Bugay) ("[W]e only pay attention to the 440 micron value."); JA 4146 (testimony of Dr. Byrn) ("You don't have to look at [the –10%] in this case."). The District Court found "both of Takeda's experts credible," JA 99, and Zydus did not present

clear and convincing evidence to the contrary. Because one skilled in the art would have no trouble discerning the boundaries of the claim, Claim 1 is not indefinite.

CONCLUSION

For all of the foregoing reasons, the judgment of the District Court should be affirmed.

Respectfully submitted,

/s/ Catherine E. Stetson

Eric J. Lobenfeld
Arlene L. Chow
HOGAN LOVELLS US LLP
875 Third Avenue
New York, NY 10022
(212) 918-3000

Catherine E. Stetson
Frederick Liu
HOGAN LOVELLS US LLP
555 Thirteenth Street, N.W.
Washington, D.C. 20004
(202) 637-5600

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Counsel for Appellees

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1. This brief complies with the type-volume limitations of Federal Rule of Appellate Procedure 32(a)(7)(B) because it contains 13,816 words.

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Catherine E. Stetson

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I hereby certify that on this 29th day of August 2013, I caused a copy of the nonconfidential version of the foregoing Brief for Appellees to be served by electronic means via the Court's CM/ECF system on all counsel registered to receive electronic notices.

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Steven J. Moore
Kelley Drye & Warren LLP
400 Atlantic Street
Stamford, CT 06901

/s/ Catherine E. Stetson
Catherine E. Stetson